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| 2352 7590 07/07/2010 OSTROLENK FABER GERB & SOFFEN 1180 AVENUE OF THE AMERICAS NEW YORK, NY 100368403 | | | | |
| EXAMINER ZAREK, PAUL E | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/532,033

Applicant(s)

VORS ET AL.

Examiner

Paul Zarek

Art Unit

1628

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 7-11, 14-17 and 20-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-5, 7-11, 14-17 and 20-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB06)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Claims

1. Claims 22 and 23 have been added by the Applicant in correspondence filed on 04/06/2010. Claims 2-5, 7-11, 14-17, and 20-23 are currently pending. This is the third Office Action on the merits of the claim(s) following a request for continued examination.

RESPONSE TO ARGUMENTS

2. Claims 2-4, 14, and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al. (International Application no. WO 00/46184). Claims 16, 5, 7-11, and 17, 20, and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett (Goodman & Gillman, The Pharmaceutical Basis of Therapeutics, 10th ed., 2001). Applicants traversed this rejection on the grounds that the applied prior art does not teach or fairly represent the claimed invention. Specifically, Applicants contend that while *Candida albicans* and *Aspergillus fumigatus* belong to the phylum Ascomycota, this phylum contains a large number and diverse array of fungi such that an agent that is effective against one fungus would not necessarily be effective against all or most other fungi, especially fungi that belong to different subphyla, as is the case with *C. albicans* and *A. fumigatus*. Applicants argue that while it may be “obvious to try” the agents disclosed in Charles, et al., for the treatment of the claimed fungi, the “obvious to try” rationale is not sufficient to establish a *prima facie* case of obviousness. Moreover, Applicants assert that Charles, et al., do not teach combining the compounds contained therein with another antifungal compound (such as itraconazole or

fluconazole) wherein the combination of the two possess allegedly synergistic effects, as shown in the instant specification (Table 6). Respectfully, Examiner does not find Applicants' arguments persuasive.

3. Charles, et al., disclose all of the antifungal compounds encompassed by instant Claim 16 (pg 1, line 16 through pg 3, line 22) and explicitly disclose compounds 364 and 365 which correspond to compounds I.1 and I.2, respectively, and teach that these compounds are active against "general pathogens of . . . Ascomycete" (pg 10, lines 9-11), the phylum to which both *C. albicans* and *A. fumigatus* belong. The issue is whether the generic disclosure in Charles, et al., reasonably suggests treating *C. albicans* and *A. fumigatus* specifically. Examiner acknowledges that Ascomycetes encompass a large and diverse portion of earthly fungi. However, antifungal compounds effective against a broad spectrum of Ascomycota are well known. Indeed, Charles, et al., demonstrate that the compounds contained therein are effective against multiple species of ascomycota: *Erysiphe graminis*, *Pyricularia oryzae*, and *Leptosphaeria nodorum*, each of which belong to the same subphylum (Pezizomycotina) as *A. fumigatus*, yet belong in distinct classes (Leotiomyces, Sordariomyces, and Dothideomyces, respectively). Furthermore, Charles, et al., are not the only group disclosing that a single class of compounds is effective against a broad array of ascomycetes. Indeed, Nieto-Roman, et al. (International Application no. WO 01/049666; English equivalent: US PreGrant Publication no. 2003/0191113, already of record), teach a single class of compounds, which is similar to but not obvious over the claimed compounds, is effective against numerous fungi, many of which are ascomycetes (paragraphs 0215-0234), including *C. albicans* and *A. fumigatus* (paragraph 0248). McGinnis and Pasarell (Journal of Clinical Microbiology, 1998, already of record) disclose that itraconazole is effective

against a wide variety of ascomycetes as well (Table I). Examiner notes that Applicants have not disagreed with Examiner's interpretation of Nieto-Roman, et al., or McGinnis and Pasarell.

Thus, one of ordinary skill in the art would reasonably expect that the compounds disclosed in Charles, et al., would be effective against a wide variety of fungi, including *C. albicans* and *A. fumigatus*, notwithstanding their different classifications.

4. Applicants' arguments regarding the alleged synergy between compounds I.1 or I.2 and fluconazole (II.1) or itraconazole (II.2) are unpersuasive. Each of the four compounds (I.1, I.2, II.1, and II.2) was known to be effective against *C. albicans* and *A. fumigatus*. Hence, an additive effect between compounds of formula I and the additional antifungal (II) would have been expected by the art worker. The data shown on Table 6 demonstrate that it was unpredictable which compounds possess a synergistic effect and which do not. In addition to the presence of both compound I.1 and either fluconazole or itraconazole, the medium in which the fungi grow appears to play a role as synergy is seen with the combination of I.1 and fluconazole in rich medium, but the combination is merely additive in minimal medium. Thus, Applicants have not demonstrated the unexpected result of synergy across the entire scope of the claims. For these reasons, the rejections of Claims 2-4, 14, and 15 under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., and of Claims 16, 5, 7-11, and 17, 20, and 21 under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett, are maintained.

5. Newly added Claims 22 and 23 are examined on their merits and the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 103

6. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.
7. Claims 22 and 23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al. (above), in view of Bennett (above)
8. Newly added Claims 22 and 23 are drawn to a method of treating *C. albicans* or *A. fumigatus* infections in humans comprising administration of compound I.1 in combination with fluconazole or itraconazole, respectively.
9. Charles, et al., and Bennett were described previously and above. Briefly, these art render *prima facie* obvious a method of treating *C. albicans* or *A. fumigatus* infections in humans comprising administration of compound I.1 and either fluconazole or itraconazole. Applicants' suggestion of unexpected synergy is not persuasive due to the fact that such synergy does not occur across the entire scope of the claimed invention. Specifically, Table 6 of the instant disclosure illustrates that the medium in which the fungi grows plays a significant role in whether the interaction between compound I.1 and fluconazole/itraconazole is synergistic or merely additive.

Conclusion

10. Claims 2-5, 7-11, 14-17, 20 and 21 remain rejected. Newly added Claims 22 and 23 are rejected.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628